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TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

047763-5010

U.S. Application No.

Unassigned

International Application. No.

International Filing Date

Priority Date Claimed

PCT/AU98/00071

06 February 1998

07 February 1997

Title of Invention

**DIAGNOSIS OF DISEASE USING TEARS**

Applicants For DO/EO/US

**Carol MORRIS, Mark WILLCOX, Bradley WALSH, Ben HERBERT, Mark MOLLOY, Andrew Arthur GOOLEY and Keith Leslie WILLIAMS**

Applicants herewith submit to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(I).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
  - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
  - b. ☐ has been transmitted by the International Bureau.
  - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
  - a. ☒ are transmitted herewith (required only if not transmitted by the International Bureau).
  - b. ☐ have been transmitted by the International Bureau.
  - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventors (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11. to 14. below concern other document(s) or information included:**

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☒ Other items or information:
  - a. ☒ WIPO Publication WO98/35229
  - b. ☒ International Search Report
  - c. ☐ International Preliminary Examination Report

U.S. APPLICATION NO. Unassigned	INTERNATIONAL APPLICATION NO. PCT/AU98/00071	ATTORNEY DOCKET NUMBER 047763-5010
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15. [X] The following fees are submitted:

**Basic National Fee (37 CFR 1.492(a)(1)-(5)):**

Search Report has been prepared by the EPO or JPO.....\$840.00

International preliminary examination fee paid to

USPTO (37 CFR 1.482).....\$670.00

No international preliminary examination fee paid to

USPTO (37 CFR 1.482) but international search fee  
paid to USPTO (37 CFR 1.445(a)(2)).....\$760.00

Neither international preliminary examination fee

(37 CFR 1.482) nor international search fee

(37 CFR 1.445(a)(2)) paid to USPTO.....\$970.00

International preliminary examination fee paid to USPTO

(37 CFR 1.482) and all claims satisfied provisions

of PCT Article 33(2)-(4).....\$96.00

**ENTER APPROPRIATE BASIC FEE AMOUNT = \$ 970.00**

Surcharge of \$130.00 for furnishing the oath or declaration later than

[ ] 20 [ ] 30 months from the earliest claimed priority date

(37 CFR 1.492(e)).

Claims	Number Filed	Number Extra	Rate	
Total Claims	12 - 20 =	0	X \$18.00	\$
Independent Claims	4 - 3 =	1	X \$78.00	\$ 78.00
Multiple dependent claim(s) (if applicable)			+\$260.00	\$

**TOTAL OF ABOVE CALCULATIONS = \$ 1,048.00**

Reduction by 1/2 for filing by small entity, if applicable. Verified

Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28)

**SUBTOTAL = \$ 1,048.00**

Processing fee of \$130.00 for furnishing the English translation later

than [ ] 20 [ ] 30 months from the earliest claimed priority date

(37 CFR 1.492(f)).

**TOTAL NATIONAL FEE = \$ 1,048.00**

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The

assignment must be accompanied by an appropriate cover sheet

(37 CFR 3.28, 3.31).

\$40.00 per property

**TOTAL FEES ENCLOSED = \$1,048.00**

Amount to be

refunded

charged

\$

\$

- a. [X] A check in the amount of **\$1,048.00** to cover the above filing fees is enclosed.
- b. [ ] Please charge my Deposit Account No. 50-0310 in the amount of \$-  
to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. [X] **Except** for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 CFR §1.16 and §1.17 which may be required, or credit any overpayment to Deposit Account No. 50-0310.

Customer No. 009629

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 Reg. No. 30,988

Submitted: August 6, 1999

PATENT  
ATTORNEY DOCKET NO.: 047763-5010

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

**Carol Morris, *et al.***

Application No.: Unassigned

(National Stage Application of

PCT/AU98/00071 filed February 6, 1998)

Filed: August 6, 1999

For: **DIAGNOSIS OF DISEASE USING TEARS**

**ATTN: BOX PCT**

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

**PRELIMINARY AMENDMENT**

Prior to the examination of the above-identified application on the merits, please amend the application as follows:

**IN THE CLAIMS:**

Please amend the claims as follows:

**Claim 5, line 1**, change "any one of claims 1 to 4" to --claim 1--.

**REMARKS**

No prohibited new matter has been introduced by this Preliminary Amendment, which is being submitted to clarify the claims, and to remove the multiple dependency from the claims.

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If there are any additional fees due in connection with the filing of this Preliminary Amendment, please charge the fees to our Deposit Account No. 50-0310.

Respectfully submitted

**MORGAN, LEWIS & BOCKIUS LLP**

By: Elizabeth C. Weimer  
for Reid G. Adler Reg. No. 744,428  
Reg. No. 30,988

Dated: August 6, 1999

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## Diagnosis of Disease using Tears

### Technical Field

The present invention relates generally to diagnosis of disease in animals including humans by detecting disease markers in tears.

### 5 Background Art

The early detection or prediction of disease in humans and animals is often important for initiating appropriate medical management of the disease. In diseases like cancer and genetic disorders, early detection can often result in successful control or treatment of these conditions. In order to  
10 carry out early detection of disease, screening methods that are simple to carry out and do not involve invasive procedures are desirable.

Presently, analyses of bodily fluids like blood, plasma, serum, urine and cerebrospinal fluid are used to screen for disease indicators. Apart from urine, these fluids require medical intervention to be obtained involving  
15 some discomfort and risk to the patient. Other bodily excretions and fluids, however, have not been considered to be of use for general screening for disease.

In traditional medicine there is a well established discipline known as Iridology whereby health/disease status is diagnosed by examination of the  
20 eye. Currently, examination of the eye or eye fluids (eg tears) has not been used to diagnose disease (other than specific eye disease) or malfunction in conventional medicine or veterinary practice.

The present inventors have made the surprising discovery that tears can be analysed to detect markers in the form of proteins that can be used as  
25 indicators of disease in animals.

### Disclosure of Invention

In a first aspect, the present invention consists in a method of screening or detecting non-ocular disease in an animal comprising obtaining a tear sample from the animal and analysing the tear sample for an indicator  
30 or marker of the non-ocular disease.

In a preferred embodiment, the present invention consists in a method of screening or detecting non-ocular disease in an animal comprising the steps:

- (a) obtaining a tear sample from the animal;
- 35 (b) separating biomolecules present in the tear sample; and

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(c) detecting for the presence or absence of one or more biomolecules such that the presence or absence of the one or more biomolecules being an indicator or marker of a disease state in the animal.

Preferably, the animal is a human subject. It will be appreciated, however, that the present invention is also suitable for veterinary situations.

The non-ocular disease may be any disease that can be detected by the presence of a biological marker excreted with, or found in, tears. It will be appreciated that such diseases would include cancer and genetic disorders. Such diseases include breast and prostate cancer.

In a preferred embodiment, the disease marker is a protein, preferably a protein having a N-terminal sequence selected from:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG:

WDPKE: and

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL.

More preferably, the disease marker is the protein:

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL, or part thereof.

In a further preferred form, the marker is a protein or proteins detected by separating the tear sample by a chromatographic technique. It will be appreciated that after separation, proteins can be identified by labelling the proteins using direct or indirect techniques known to the art. Any type of electrophoresis can be used, however, two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) is particularly suitable to separate proteins from tear fluids. Protein banding and/or spot patterns from analyses of tears from patients and normal individuals using this method can be compared to detect abnormalities or differences. As particular protein markers will appear in known positions in a 2D-PAGE gel, for example, the presence or absence of a protein marker in a tear sample may be indicative of a disease state or a potential problem for the patient. Furthermore, a change in the relative position of a marker after the chromatography may indicate changes in that protein from the patient. This may also be relevant in diagnosis of disease as it may indicate a mutation or change in the protein or modifications which can cause or lead to a disease state.

It will be appreciated that other methods presently available to detect proteins in biological samples would also be useful to analyse tear samples

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for the presence of disease markers. Suitable methods include direct testing of a tear sample (neat or in a concentrated form, for example) using labelled probes in an immunoassay or radioimmunoassay. Antibodies can be prepared against proteins found in tears that are markers for disease states and used in such assays. The important discovery that tears may include protein markers indicative of a disease state will allow such assays to be developed.

The detection of one or more disease markers in a tear sample from a patient may alert the physician of a predisposition for disease in that patient. The present invention may be used to screen patients in a high risk group for a particular disease or be used to place patients in a particular risk group. The patient may be monitored further by other more invasive methods to confirm diagnosis or appropriate treatment can be started.

In a second aspect, the present invention consists in a protein marker detectable in tears having a N-terminus selected from:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG;

WDPKE; and

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN  
QSHRTLKNFG LMMHTVYDSI WCNL.

Preferably, the protein marker detectable in tears includes the amino acid sequence:

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN  
QSHRTLKNFG LMMHTVYDSI WCNL, or part thereof.

It will be appreciated that antibodies may be generated to the protein markers according to this invention which could be used to detect the proteins in tears by suitable assays known to the art.

In a third aspect, the present invention consists in isolated nucleic acid molecules encoding the protein markers according to the second aspect of the present invention.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

In order that the present invention may be more clearly understood, preferred forms will be described with reference to the following examples.

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Modes for Carrying Out the Invention

## METHODS

## Sample preparation

5 Reflex tears were collected using glass microcapillary tubes from 12 non-contact lens wearing male and female humans and pooled. Reflex tears were stimulated by gently rubbing the nasal mucosa with a cotton wool tipped bud. Care was taken to minimise ocular surface contact during the collection. As an added precaution, examination of the ocular surface using slit lamp biomicroscopy and fluorescein was conducted on all subjects after  
10 tear collection to discount the possibility of ocular surface damage. Each sample was centrifuged at 2.000 g for 10 min to remove cell debris, then recovered and stored at -80°C prior to 2D-PAGE.

Two different batches of tears from different groups of individuals were examined by analytical and preparative 2-dimensional electrophoresis.

## 15 Two-dimensional electrophoresis

For analytical gels a 7 microliter of sample was thawed and added to 500 microliter of rehydration solution (8M Urea, 4% CHAPS, 100 mM DTT and 40 mM Tris). The solution was introduced into a sealed 2 ml plastic tissue culture pipette containing a single 18 cm Immobiline DryStrip  
20 (covering the range approximately pH 3.5-10). The strip was rehydrated at room temperature for 24 hours.

Preparative gels were prepared in the same manner, although 250 microliter of sample was loaded. The sample was lyophilised before dissolving in the 500 microliter of rehydration solution. The first dimension, isoelectric focussing (IEF), was carried out using a Pharmacia Multiphor II  
25 with a DryStrip Kit; power was supplied using a Consort 5000 V power supply and cooling water at 20°C was supplied by a Pharmacia Multitemp III. Table 1 gives the running conditions for the IEF. After IEF, the strips were stored at -80°C until required for the second dimension.

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Table 1. Running conditions for the first dimension IEF

Phase	V	mA (max)	W (Max)	Time (h)	Vh
1	300	1.0	5.0	5	1,500
2	1000	1.0	5.0	10	10,000
3	3500	1.0	5.0	10	35,000
4	5000	1.0	5.0	<100	<500,000

5 Prior to the second dimension, the IPG strips were equilibrated for 2 X 10 minutes. For the first 10 min. the strips were placed in 6 M urea, 2% SDS, 20% glycerol 0.375 M Tris/HCl, pH 8.8 and 2% DTT. For the second 10 min, that solution was discarded and replaced by 6 M urea, 2% SDS, 20% glycerol 0.375 M Tris/HCl, pH 8.8 and 2.5% iodoacetamide.

10 Second dimension gels were run using the Bio-Rad Protean II Multicell system. The gels were 1.5 mm thick, 8-18% T gradients, and were crosslinked with PDA at 2.5% C. The gel and anode buffers were 0.375 M tris/HCl, pH 8.8. Cathode buffer was 192 mM glycine/tris pH 8.3, 0.1% (w/v) SDS and 0.001% (w/v) Bromophenol blue. The equilibrated IPG strips were  
15 embedded on the top of the SDS-PAGE gel using molten 1% (w/v) agarose in cathode buffer. Pharmacia low molecular weight standards were loaded in a single lane at one side of each gel. Gels were run at 25 mA per gel overnight, until the Bromophenol blue front had traversed the gel.

The completed analytical 2D gels were stained with an ammoniacal silver stain. Preparative gels were transferred to PVDF by standard methods.  
20 Proteins in preparative gels were visualised by staining with 0.1% (w/v) Coomassie Blue in 40% (v/v) methanol, after transfer to PVDF membranes.

#### N-Terminal Sequencing

Protein spots were excised from the PVDF membrane and loaded into a membrane-compatible Hewlett-Packard cartridge. Sequencing was  
25 conducted with a Model G1005A (Hewlett-Packard, CA) sequenator.

#### RESULTS

Table 2 shows the results of N-terminal sequencing of 10 spots from a single preparative 2D gel transferred to PVDF membrane and stained with Coomassie Blue. Eight of the spots gave N-terminal sequences, with only  
30 spot 5 N-terminally blocked. This blocked protein was identified as human Zn-alpha-2 Glycoprotein by amino acid analysis matching to the database.

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Five different proteins were identified on the basis of N-terminal sequencing, with two proteins being represented in two different spots (1 & 2 being the same protein; 3 & 4 being the same protein) and one protein, the lipocalin Von Ebner's Gland Protein, being present in both intact and a N-terminally processed form. The present inventors believe this is the first report of N-terminal processing of Von Ebner's Gland Protein.

In all, seven different proteins were observed. Four of these proteins are known: human Cystatin S (spots 3 & 4); Human Von Ebner's Gland protein (spots 11 & 12) Human Zn-alpha-2 Glycoprotein (spot 5); and human lactotransferrin (spot 14).

Three new proteins were identified by this method. One (spot 9) is a protein of 74 amino acids with an apparent SDS-PAGE mass of 8 kDa and a predicted mass of 8.506 Da and is closely related to the uteroglobins. The Asparagine at position 50, while in the N-glycosylation motif Asn-Gln-Ser, is not glycosylated. The Cys at positions 4, 47 and 72 were identified as the acrylamide adducts of reduced Cysteine.

Uteroglobins are potent inhibitors of phospholipase A2 and are proteins of approximately 70 amino acids that form antiparallel disulfide-linked dimers. Examples of members of the uteroglobins are human mammaglobin (Swiss-Prot Q13296) and rat prostatic steroid-binding protein C3 (Swiss Prot P02780). These proteins are putative markers for breast and prostate cancer, respectively. Based on these similar proteins, the present inventors propose that the unknown protein spot 9 is a marker for a human cancer. Spot 9 was abundant and observed as one of three spots in a train of differing isoelectric point in one of the tear samples and weakly present in the other.

The second new protein was represented in at least 5 isoforms of different pI. Two of these were N-terminally sequenced and gave the sequence commencing EDASS (EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDLAG) (spots 1 & 2).

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Table 2. Identification of Human Reflex Tears proteins by N-terminal sequence tagging and amino acid analysis

Spot No.	pI	Mw (k)	Sequence Tag	Identification
1	5.0	25	EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG	unknown -
2	4.4	25	EDASS	As for No. 1
3	4.6	14	SSSKE	Human Cystatin S
4	4.8	14	SSSKE	As for No. 3
5	5.2	40	N-terminally blocked*	Human Zn-alpha-2-glycoprotein
9	5.1	10	<sup>1</sup> DSGCKLLEDMVEK	Similarity with Human Mammaglobin & Rat Steroid-binding proteins
10	8.0	14	WDPKE	Unknown
11	5.1	18	HHLLASDEE	Human Von Ebner's Gland Protein
12	5.3	18	^SDEE	Von Ebner's Gland Protein
14	8.5	80	GRRR	Human lactotransferrin

- 5 \* Identified on the basis of amino acid composition matching using the AACompIdent2 program in ExPASy (Expert Protein Analysis System) on the world wide web at <http://expasy.hcuge.ch/ch2d/aacomp2.html>.

<sup>1</sup> 74 Residues sequenced

10 ..... 10.... ... 20.... .....30..... ..40..... .....50  
 DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN  
 ..... 60..... 70....  
 QSHRTLKNFG LMMHTVYDSI WCNL

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While the identification of spot 1 protein remains unknown it is interesting that these first N-terminal amino acids showed some sequence similarity (>40% sequence identity) to the N-terminal regions of the rat huntingtin associated protein (Swiss-Prot P54256, a protein associated with  
5 Huntington's disease and hence a possible disease marker) and the californian sea hare Synaptotagmin (Swiss Prot P41823, a protein which binds acidic phospholipids and is possibly relevant to tear activity in phospholipid binding).

10 The third new protein WDPKE (spot 10) has no related proteins in the database.

By examination of the trains of spots it was possible to identify changes in the post-translational modification status of some proteins between the two samples of tears.

15 The results presented have identified three new proteins, one of which is related to known cancer markers, and another is differentially processed protein in tears. The present inventors have found differences in levels of the respective proteins as well as in their modification status. These discoveries indicate new targets for development of diagnostic reagents for assessing disease status. The present invention is an important new  
20 approach to the development of diagnosis as it is non-invasive and applicable to not only humans but also animals.

25 It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

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## CLAIMS:

1. A method of screening or detecting non-ocular disease in an animal, the method comprising obtaining a tear sample from the animal and analysing the tear sample for an indicator or marker of the non-ocular disease, wherein the indicator or marker is a protein having a N-terminal amino acid sequence selected from the group consisting of:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG;

WDPKE; and

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL.

2. The method according to claim 1 wherein the protein includes the amino acid sequence:

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL, or part thereof.

3. A method of screening or detecting non-ocular disease in an animal, the method comprising the steps of:

(a) obtaining a tear sample from the animal;

(b) separating biomolecules present in the tear sample; and

(c) detecting for the presence or absence of one or more biomolecules

such that the presence or absence of the one or more biomolecules being an indicator or marker of a disease state in the animal, wherein the one or more biomolecules are one or more proteins having a N-terminal amino acid sequence selected from the group consisting of:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG;

WDPKE; and

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL.

4. The method according to claim 3 wherein the protein includes the amino acid sequence:

DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN

QSHRTLKNFG LMMHTVYDSI WCNL, or part thereof.

5. The method according to any one of claims 1 to 4 wherein the non-ocular disease is selected from cancers and genetic disorders.

6. The method according to claim 5 wherein the cancer is breast or prostate cancer.

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7. The method according to claim 3 wherein the separating step (b) is by a chromatographic or an electrophoretic technique.

8. The method according to claim 7 wherein the electrophoretic technique is two-dimensional polyacrylamide gel electrophoresis (2D-PAGE).

5 9. The method according to claim 3 wherein the detecting step (c) involves direct or indirect analysis using labelled probes specific for the disease indicator or marker in an immunoassay or radioimmunoassay.

10. An isolated protein detectable in tears having an amino acid N-terminus selected from the group consisting of:

10 EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG;

WDPKE; and

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN  
QSHRTLKNFG LMMHTVYDSI WCNL.

11. An isolated protein detectable in tears including the amino acid sequence:

15 DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN  
QSHRTLKNFG LMMHTVYDSI WCNL, or part thereof.

12. An isolated nucleic acid molecule encoding any one of the proteins according to claim 10.

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AMENDED SHEET - IPEA/AU

# COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark Office

ATTORNEY DOCKET NO.: 47763-

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

## DIAGNOSIS OF DISEASE USING TEARS

the specification of which:

is attached hereto; or

was filed as United States application Serial No. \_\_\_\_\_ on \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable); or

was filed as PCT international application Number PCT/AU98/00071 on February 6, 1998 and was amended under PCT Article 19 on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended to any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office information which is material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

### PRIOR FOREIGN APPLICATION(S):

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Australia	PO5009	7 February 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-50

I hereby claim the benefits under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

U.S. PROVISIONAL APPLICATIONS

U.S. PROVISIONAL APPLICATION NO.

U.S. FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or §365(c) of any PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to me to be material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT

U.S. APPLICATIONS

STATUS (Check One)

U.S. APPLICATION NO.

U.S. FILING DATE

PATENTED

PENDING

ABANDONED

**POWER OF ATTORNEY:** As a named inventor, I hereby appoint the registered practitioners of Morgan, Lewis & Bockius LLP included in the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number.

Customer Number: 009629

Direct Telephone Calls To:  
(name and telephone number)

Reid G. Adler  
202-467-7756



Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-50

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

FULL NAME OF SOLE  
OR FIRST INVENTOR

Carol MORRIS

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

AUX

COUNTRY OF  
CITIZENSHIP

Australia

POST OFFICE ADDRESS

9 Chuter Street, North Sydney, New South Wales, 2060, Australia

FIRST OR SOLE INVENTOR'S SIGNATURE

Carol A. Morris

DATE

27/09/99

FULL NAME OF  
SECOND INVENTOR

Mark WILLCOX

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

AUX

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

85 College Street, Balmain, New South Wales, 2041, Australia

SECOND INVENTOR'S SIGNATURE

DATE

FULL NAME OF THIRD  
INVENTOR

Shirley BOLIS

RESIDENCE &  
CITIZENSHIP

Griffith, Australia

AUX

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

8/53 McMillan Crescent, Griffith, ACT, 2603, Australia

THIRD INVENTOR'S SIGNATURE

DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763

FULL NAME OF FOURTH INVENTOR	Bradley WALSH	
RESIDENCE & CITIZENSHIP	New South Wales, Australia AUX	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia AUX	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	3 Douglas Avenue <del>25 Marbella Street</del> , North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE 13/10/99
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia MI	COUNTRY OF CITIZENSHIP
POST OFFICE ADDRESS	54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia	
SIXTH INVENTOR'S SIGNATURE		SEE NEXT DEC FOR ADDRESS CHANGE OF 6TH INVENTOR
FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia AUX	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	15 Katina St, Turrumanna, NSW, 2074, <del>14 Vinniera Road, Eastwood, New South Wales, 2122</del> , Australia	
SEVENTH INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s) [X ] Yes [ ] No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-50

FULL NAME OF  
EIGHTH INVENTOR

Keith Leslie WILLIAMS

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

AUX

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia

EIGHTH INVENTOR'S SIGNATURE

DATE

Listing of Inventors Continued on attached page(s)

[ ] Yes

[X] No

658011 600/3660

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

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RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE

FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE

FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia	
SIXTH INVENTOR'S SIGNATURE		DATE

FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	14 Vimera Road, Eastwood, New South Wales, 2122, Australia	
SEVENTH INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

# COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark Office

ATTORNEY DOCKET NO.: 47763-5

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

## DIAGNOSIS OF DISEASE USING TEARS

the specification of which:

is attached hereto; or

was filed as United States application Serial No. \_\_\_\_\_ on \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable); or

was filed as PCT international application Number PCT/AU98/00071 on February 6, 1998 and was amended under PCT Article 19 on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended to any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office information which is material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

### PRIOR FOREIGN APPLICATION(S):

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Australia	PO5009	7 February 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

I hereby claim the benefits under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

U.S. PROVISIONAL APPLICATIONS

U.S. PROVISIONAL APPLICATION NO.	U.S. FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or §365(c) of any PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to me to be material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT

U.S. APPLICATIONS		STATUS (Check One)		
U.S. APPLICATION NO.	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

**POWER OF ATTORNEY:** As a named inventor, I hereby appoint the registered practitioners of Morgan, Lewis & Bockius LLP included in the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number.

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(name and telephone number)

Reid G. Adler  
202-467-7756

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
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ATTORNEY DOCKET NO.: 47763-50

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FULL NAME OF SOLE OR FIRST INVENTOR	Carol MORRIS	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	9 Chuter Street, North Sydney, New South Wales, 2060, Australia	
FIRST OR SOLE INVENTOR'S SIGNATURE		DATE
FULL NAME OF SECOND INVENTOR	Mark WILLCOX	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	85 College Street, Balmain, New South Wales, 2041, Australia	
SECOND INVENTOR'S SIGNATURE		DATE
FULL NAME OF THIRD INVENTOR	Shirley BOLIS	
RESIDENCE & CITIZENSHIP	Griffith, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	8/53 McMillan Crescent, Griffith, ACT, 2603, Australia	
THIRD INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

FULL NAME OF FOURTH INVENTOR	Bradley WALSH	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	<del>New South Wales, Australia</del> Ann Arbor, Michigan, USA	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	<del>54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia</del> 915 WEST HURON, ANN ARBOR, MI, 48103, USA.	
SIXTH INVENTOR'S SIGNATURE <i>M. Molloy</i>		DATE 22/9/
FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	14 Vimiera Road, Eastwood, New South Wales, 2122, Australia	
SEVENTH INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No



Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-4

FULL NAME OF EIGHTH INVENTOR	Keith Leslie WILLIAMS	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia	
EIGHTH INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s)    ☐ Yes    ☒ No

66807 " 50029660

# COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark Office

ATTORNEY DOCKET NO.: 47763-4

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

## DIAGNOSIS OF DISEASE USING TEARS

the specification of which:

is attached hereto; or

was filed as United States application Serial No. \_\_\_\_\_ on \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable); or

was filed as PCT international application Number PCT/AU98/00071 on February 6, 1998 and was amended under PCT Article 17 on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office information which is material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56.

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### PRIOR FOREIGN APPLICATION(S):

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Australia	PO5009	7 February 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

I hereby claim the benefits under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

U.S. PROVISIONAL APPLICATIONS

U.S. PROVISIONAL APPLICATION NO.	U.S. FILING DATE

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PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT

U.S. APPLICATIONS		STATUS (Check One)		
U.S. APPLICATION NO.	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

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(name and telephone number)

Reid G. Adler  
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Combined Declaration For Patent Application and Power of Attorney - (Continued)  
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ATTORNEY DOCKET NO.: 47763-5

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FULL NAME OF SOLE OR FIRST INVENTOR	Carol MORRIS	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	9 Chuter Street, North Sydney, New South Wales, 2060, Australia	
FIRST OR SOLE INVENTOR'S SIGNATURE		DATE
FULL NAME OF SECOND INVENTOR	Mark WILLCOX	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	22 85, College Street, Balmain, New South Wales, 2041, Australia	
SECOND INVENTOR'S SIGNATURE		DATE 24/9/99
FULL NAME OF THIRD INVENTOR	Shirley BOLIS	
RESIDENCE & CITIZENSHIP	Griffith, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	8/53 McMillan Crescent, Griffith, ACT, 2603, Australia	
THIRD INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s) [ X ] Yes [ ] No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

FULL NAME OF FOURTH INVENTOR	Bradley WALSH	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia	
SIXTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	14 Vimiera Road, Eastwood, New South Wales, 2122, Australia	
SEVENTH INVENTOR'S SIGNATURE		DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-

FULL NAME OF EIGHTH INVENTOR			Keith Leslie WILLIAMS		
RESIDENCE & CITIZENSHIP		New South Wales, Australia			COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS		23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia			
EIGHTH INVENTOR'S SIGNATURE					DATE

Listing of Inventors Continued on attached page(s)    ☐ Yes    ☒ No

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Patent and Trademark Office

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### PRIOR FOREIGN APPLICATION(S):

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Australia	PO5009	7 February 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-50

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U.S. PROVISIONAL APPLICATIONS

U.S. PROVISIONAL APPLICATION NO.

U.S. FILING DATE

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PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT

U.S. APPLICATIONS

STATUS (Check One)

U.S. APPLICATION NO.

U.S. FILING DATE

PATENTED

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Combined Declaration For Patent Application and Power of Attorney - (Continued)  
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FULL NAME OF SOLE  
OR FIRST INVENTOR

**Carol MORRIS**

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

COUNTRY OF  
CITIZENSHIP

Australia

POST OFFICE ADDRESS

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FIRST OR SOLE INVENTOR'S SIGNATURE

DATE

FULL NAME OF  
SECOND INVENTOR

**Mark WILLCOX**

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

85 College Street, Balmain, New South Wales, 2041, Australia

SECOND INVENTOR'S SIGNATURE

DATE

FULL NAME OF THIRD  
INVENTOR

**Shirley BOLIS**

RESIDENCE &  
CITIZENSHIP

Griffith, Australia

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

8/53 McMillan Crescent, Griffith, ACT, 2603, Australia

THIRD INVENTOR'S SIGNATURE

*SBOLIS*

DATE  
23<sup>rd</sup> Sept 1990

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
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ATTORNEY DOCKET NO.: 47763-50

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FOURTH INVENTOR'S SIGNATURE					DATE
FULL NAME OF FIFTH INVENTOR			Ben HERBERT		
RESIDENCE & CITIZENSHIP			New South Wales, Australia		COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS			25 Marcella Street, North Epping, New South Wales, 2121, Australia		
FIFTH INVENTOR'S SIGNATURE					DATE
FULL NAME OF SIXTH INVENTOR			Mark MOLLOY		
RESIDENCE & CITIZENSHIP			New South Wales, Australia		COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS			54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia		
SIXTH INVENTOR'S SIGNATURE					DATE
FULL NAME OF SEVENTH INVENTOR			Andrew Arthur GOOLEY		
RESIDENCE & CITIZENSHIP			New South Wales, Australia		COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS			14 Vimiera Road, Eastwood, New South Wales, 2122, Australia		
SEVENTH INVENTOR'S SIGNATURE					DATE

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Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-5

FULL NAME OF  
EIGHTH INVENTOR

Keith Leslie WILLIAMS

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia

EIGHTH INVENTOR'S SIGNATURE

DATE

Listing of Inventors Continued on attached page(s)    ☐ Yes    ☒ No

09367009 10399  
5580TF 50049560

# COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark Office

ATTORNEY DOCKET NO.: 47763-5

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

## DIAGNOSIS OF DISEASE USING TEARS

the specification of which:

is attached hereto; or

was filed as United States application Serial No. \_\_\_\_\_ on \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable); or

was filed as PCT international application Number PCT/AU98/00071 on February 6, 1998 and was amended under PCT Article 19 on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

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I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

### PRIOR FOREIGN APPLICATION(S):

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Australia	PO5009	7 February 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

ATTORNEY DOCKET NO.: 47763-50

I hereby claim the benefits under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

U.S. PROVISIONAL APPLICATIONS

U.S. PROVISIONAL APPLICATION NO.	U.S. FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or §365(c) of any PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to me to be material to the patentability of claims presented in this application in accordance with Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT

U.S. APPLICATIONS		STATUS (Check One)		
U.S. APPLICATION NO.	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

**POWER OF ATTORNEY:** As a named inventor, I hereby appoint the registered practitioners of Morgan, Lewis & Bockius LLP included in the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number.

Customer Number: 009629

Direct Telephone Calls To:  
(name and telephone number)

Reid G. Adler  
202-467-7756

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
(includes Reference to PCT International Applications)

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

FULL NAME OF SOLE  
OR FIRST INVENTOR

**Carol MORRIS**

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FIRST OR SOLE INVENTOR'S SIGNATURE

DATE

FULL NAME OF  
SECOND INVENTOR

**Mark WILLCOX**

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COUNTRY OF  
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POST OFFICE ADDRESS

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SECOND INVENTOR'S SIGNATURE

DATE

FULL NAME OF THIRD  
INVENTOR

**Shirley BOLIS**

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CITIZENSHIP

Australia

POST OFFICE ADDRESS

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THIRD INVENTOR'S SIGNATURE

DATE

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No

Combined Declaration For Patent Application and Power of Attorney - (Continued)  
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ATTORNEY DOCKET NO.: 47763-50

FULL NAME OF FOURTH INVENTOR	Bradley WALSH	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE 20/7/94
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia	
SIXTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	14 Vimiera Road, Eastwood, New South Wales, 2122, Australia	
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FULL NAME OF  
EIGHTH INVENTOR

Keith Leslie WILLIAMS

RESIDENCE &  
CITIZENSHIP

New South Wales, Australia

COUNTRY OF  
CITIZENSHIP  
Australia

POST OFFICE ADDRESS

23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia

EIGHTH INVENTOR'S SIGNATURE

DATE

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652071-600/9560



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OR FIRST INVENTOR

**Carol MORRIS**

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CITIZENSHIP

New South Wales, Australia

COUNTRY OF  
CITIZENSHIP

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POST OFFICE ADDRESS

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FIRST OR SOLE INVENTOR'S SIGNATURE

DATE

FULL NAME OF  
SECOND INVENTOR

**Mark WILLCOX**

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SECOND INVENTOR'S SIGNATURE

DATE

FULL NAME OF THIRD  
INVENTOR

**Shirley BOLIS**

RESIDENCE &  
CITIZENSHIP

Griffith, Australia

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POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE	DATE	
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE	DATE	
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
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FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	15 Katina St, Turrumurra, NSW, 2074, 14 Vimiera Road, Eastwood, New South Wales, 2122, Australia	
SEVENTH INVENTOR'S SIGNATURE	DATE	

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FULL NAME OF EIGHTH INVENTOR	Keith Leslie WILLIAMS	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	23 Nandi Avenue, Frenchs Forest, New South Wales, 2086, Australia	
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U.S. APPLICATIONS

STATUS (Check One)

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FULL NAME OF SOLE OR FIRST INVENTOR	Carol MORRIS	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	9 Chuter Street, North Sydney, New South Wales, 2060, Australia	
FIRST OR SOLE INVENTOR'S SIGNATURE	DATE	
FULL NAME OF SECOND INVENTOR	Mark WILLCOX	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	85 College Street, Balmain, New South Wales, 2041, Australia	
SECOND INVENTOR'S SIGNATURE	DATE	
FULL NAME OF THIRD INVENTOR	Shirley BOLIS	
RESIDENCE & CITIZENSHIP	Griffith, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	8/53 McMillan Crescent, Griffith, ACT, 2603, Australia	
THIRD INVENTOR'S SIGNATURE	DATE	

Listing of Inventors Continued on attached page(s)    ☒ Yes    ☐ No



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ATTORNEY DOCKET NO.: 47763-50

FULL NAME OF FOURTH INVENTOR	Bradley WALSH	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	34 Beach Street, South Curl Curl, New South Wales, 2096, Australia	
FOURTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF FIFTH INVENTOR	Ben HERBERT	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP New Zealand
POST OFFICE ADDRESS	25 Marcella Street, North Epping, New South Wales, 2121, Australia	
FIFTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SIXTH INVENTOR	Mark MOLLOY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
POST OFFICE ADDRESS	54/147 Talavera Road, Marsfield, New South Wales, 2122, Australia	
SIXTH INVENTOR'S SIGNATURE		DATE
FULL NAME OF SEVENTH INVENTOR	Andrew Arthur GOOLEY	
RESIDENCE & CITIZENSHIP	New South Wales, Australia	COUNTRY OF CITIZENSHIP Australia
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SEVENTH INVENTOR'S SIGNATURE 		DATE

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DATE

16-7-99

Listing of Inventors Continued on attached page(s)

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55307 600/9550